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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/066,506	01/31/2002	Case C. Grogan	003/243/SAP	5120

7590 08/01/2005

ATTN: MCMR-JA (Ms. Elizabeth Arwine- PATENT ATTY)
U. S. Army Medical Research and Materiel Command
504 Scott Street
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EXAMINER	
PARKIN, JEFFREY S	

ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 08/01/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/066,506	GROGAN ET AL.	
	Examiner	Art Unit	
	Jeffrey S. Parkin, Ph.D.	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *03* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 November 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-52* is/are pending in the application.

4a) Of the above claim(s) *1-18,29-31 and 35-48* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *19-28,32-34 and 49-52* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *10/15/03*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

5.0.0

Detailed Office Action

Status of the Claims

Acknowledgement is hereby made of receipt and entry of the communication received 15 November, 2004. Claims 19-28, 32-34, and 49-52 are currently under examination. Claims 1-18, 29-31, and 35-48 have been withdrawn from further consideration by the examiner, pursuant to 37 C.F.R. § 1.142(b), as being drawn to a non-elected invention.

35 U.S.C. § 112, First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Written Description

Claims 19-28, 32-34, and 49-52 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. *In re Rasmussen*, 650 F.2d 1212, 211 U.S.P.Q. 323 (C.C.P.A. 1981). *In re Wertheim*, 541 F.2d 257, 191 U.S.P.Q. 90 (C.C.P.A. 1976). *University of Rochester* v. *G. D. Searle & Co., Inc.*,, 358 F.3d 916, 69 U.S.P.Q.2d 1886 (C.A.F.C. 2004).

To satisfy the written description requirement, a patent specification must describe the claimed invention in sufficient

detail that one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention. See, e.g., *Vas-Cath, Inc., v. Mahurkar*, 935 F.2d at 1563, 19 U.S.P.Q.2d at 1116. The issue raised in this application is whether the original application provides adequate support for the broadly claimed genus of chimeric filovirus glycoproteins comprising any portion of GP1 or any portion of GP2. The claims encompass as few as one amino acid from each GP up to or including the full-length regions. For the Marburg GP, GP1 encompasses 435 amino acids while the GP2 portion encompasses 245 amino acids. For the Ebola GP, GP1 is 501 amino acids and GP2 174 amino acids. Thus, the chimeric envelope glycoprotein could encompass an inordinate number of variants. However, the disclosure only describes chimeric envelope glycoproteins wherein the carboxyl-terminus of a full-length GP1 of a first virus is fused to the amino-terminus of a full-length GP2 of a second virus. No other fusion proteins are disclosed. An applicant shows possession of the claimed invention by describing the claimed invention with all of its limitations using such descriptive means as words, structures, figures, diagrams, and formulas that fully set forth the claimed invention. *Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572, 41 U.S.P.Q.2d 1961, 1966 (Fed. Cir. 1997). The claimed invention as a whole may not be adequately described where an invention is described solely in terms of a method of its making coupled with its function and there is no described or art-recognized correlation or relationship between the structure of the invention and its function. A biomolecule sequence described only by functional characteristic, without any known or disclosed correlation between that function and the structure of the sequence, normally is not a sufficient identifying characteristic for written description purposes, even when accompanied by a method of obtaining the biomolecule of interest. *In re Bell*, 991 F.2d 781, 26 U.S.P.Q.2d 1529 (Fed. Cir. 1993). *In re Deuel*, 51 F.3d 1552, 34 U.S.P.Q.2d 1210 (Fed. Cir.

1995). A lack of adequate written description issue also arises if the knowledge and level of skill in the art would not permit one skilled in the art to immediately envisage the product claimed from the disclosed process. See, e.g., *Fujikawa v. Wattanasin*, 93 F.3d 1559, 1571, 39 U.S.P.Q.2d 1895, 1905 (Fed. Cir. 1995). The court noted in this decision that a "laundry list" disclosure of every possible moiety does not constitute a written description of every species in a genus because it would not reasonably lead those skilled in the art to any particular species.

An applicant may show possession of an invention by disclosure of drawings or structural chemical formulas that are sufficiently detailed to show that applicant was in possession of the claimed invention as a whole. An applicant may also show that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics which provide evidence that applicant was in possession of the claimed invention, i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics. For some biomolecules, examples of identifying characteristics include a nucleotide or amino acid sequence, chemical structure, binding affinity, binding specificity, and molecular weight. The written description requirement may be satisfied through disclosure of function and minimal structure when there is a well-established correlation between structure and function. Without such a correlation, the capability to recognize or understand the structure form the mere recitation of function and minimal structure is highly unlikely. In the latter case, disclosure of function alone is little more than a wish for possession; it does not satisfy the written description requirement. *Regents of the University of California v. Eli Lilly*, 119 F.3d 1559, 1566, 43 U.S.P.Q.2d 1398, 1404, 1406 (Fed. Cir. 1997), *cert. denied*, 523 U.S. 1089 (1998). *In re*

Wilder, 736 F.2d 1516, 1521, 222 U.S.P.Q. 369, 372-3 (Fed. Cir. 1984). Factors to be considered in determining whether there is sufficient evidence of possession include the level of skill and knowledge in the art, partial structure, physical and/or chemical properties, functional characteristics alone or coupled with a known or disclosed correlation between structure and function, and the method of making the claimed invention.

As noted *supra*, the disclosure only describes chimeric envelope glycoproteins wherein the carboxyl-terminus of a full-length GP1 of a first virus is fused to the amino-terminus of a full-length GP2 of a second virus. No other fusion proteins are disclosed. The disclosure fails to identify critical protective immunological determinants that can be linked together in such a manner that their properties are retained when placed within the context of a larger fusion protein. Thus, after perusing the specification, the skilled artisan would reasonably conclude that applicants were only in possession of fusion proteins comprising the following coding regions: EBOV GP1 (aa 1-501), EBOV GP2 (aa 502-676), MBGV GP1 (aa 1-435), and MBGV GP2 (aa 436-681). There is nothing in the disclosure that would lead the skilled artisan to any other combination of molecules.

Scope of Enablement

Claims 19-28, 32-34, and 49-52 are rejected under 35 U.S.C. § 112, first paragraph, because the specification does not reasonably enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims. The claims are directed toward a large genus of recombinant filovirus envelope glycoproteins comprising any portion of GP1 or any portion of GP2. Thus, the claims could encompass as few as one amino acid from each GP up to or including the full-length regions. For the Marburg GP, GP1 encompasses 435 amino acids while the GP2 portion encompasses

245 amino acids. For the Ebola GP, GP1 is 501 amino acids and GP2 174 amino acids. Thus, the chimeric envelope glycoprotein could encompass an inordinate number of variants. However, the disclosure only describes chimeric envelope glycoproteins wherein the carboxyl-terminus of a full-length GP1 of a first virus is fused to the amino-terminus of a full-length GP2 of a second virus. No other fusion proteins are disclosed. Appropriately drafted claim language directed toward these embodiments would be acceptable. However, the specification clearly fails to support the full breadth of the claimed invention.

The legal considerations that govern enablement determinations pertaining to undue experimentation have been clearly set forth. *Enzo Biochem, Inc.*, 52 U.S.P.Q.2d 1129 (C.A.F.C. 1999). *In re Wands*, 8 U.S.P.Q.2d 1400 (C.A.F.C. 1988). *Ex parte Forman* 230 U.S.P.Q. 546 (PTO Bd. Pat. App. Int., 1986). The courts concluded that several factual inquiries should be considered when making such assessments including the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in that art, the predictability or unpredictability of the art and the breadth of the claims. *In re Rainer*, 52 C.C.P.A. 1593, 347 F.2d 574, 146 U.S.P.Q. 218 (1965). The disclosure fails to provide adequate guidance pertaining to a number of these considerations as follows:

1) The disclosure fails to provide any guidance pertaining to the location of any given linear antigenic/immunogenic determinant within any given filovirus envelope glycoprotein. The specification clearly states (p. 3) that "the present invention describes a single-component bivalent vaccine protective against both Ebola and Marburg viruses". It has been well-documented in the art that most antigenic determinants consist of five to eight amino acid residues. However, the specification does not identify

any putative protective epitopes within the envelope glycoproteins of the Ebola or Marburg viruses. Thus, the skilled artisan has been asked to guess as to which "portions thereof" will contain the desired epitopes.

2) The disclosure fails to provide any guidance pertaining to the location of any given conformational antigenic/immunogenic determinant within any given filovirus envelope glycoprotein. It has also bee well-documented that many protective neutralizing epitopes are conformational in nature, requiring complex folding schemes. However, the specification fails to identify those amino acid residues that are critical for the generation of protective immune responses. Accordingly, the skilled artisan is once again being asked to identify those critical protective molecular determinants without sufficient teachings from the disclosure.

3) The disclosure fails to provide adequate guidance pertaining to the creation of chimeric proteins involving "portions thereof" that result in retention of the antigenic/immunogenic properties of the molecule. It has been well-documented in the prior art that the skilled artisan can not randomly link various epitopes together without affecting the overall properties of any given epitope (Partidos *et al.*, 1992(a)(b); Eisenlohr *et al.*, 1992; Janssen *et al.*, 1994). Joining epitopes together in a chimeric molecule frequently results in a loss of antigenicity/immunogenicity or the creation of immunodominant neoepitopes that direct the immune response away from the desired molecular determinants.

4) The disclosure fails to provide a sufficient number of working embodiments. Table 1 (p. 17) provides a description of the chimeric envelope glycoproteins generated. In each construct, the carboxyl-terminus of the full-length GP1 was linked to the amino-terminus of a full-length GP2. The specification fails to provide any working embodiments where chimeric envelopes were created comprising "portions thereof".

5) The state-of-the-art vis-à-vis the identification of protective

filovirus epitopes is one of unpredictability. As set forth throughout the specification, the present invention is directed toward immunogenic compositions that can provide a protective immune response against both the Ebola and Marburg viruses. However, the state-of-the-art clearly illustrates that the identification of suitable protective epitopes has been problematic (Ayato *et al.*, 2003). This is not surprising considering that the correlates of human protection remain to be elucidated and that there are no adequate animal models with which to assess vaccine efficacy.

Accordingly, when all the aforementioned factors are considered *in toto*, it would clearly require undue experimentation from the skilled artisan to practice the claimed invention.

Correspondence

The Art Unit location of your application in the Patent and Trademark Office has changed. To facilitate the correlation of related papers and documents for this application, all future correspondence should be directed to **art unit 1648.**

Any inquiry concerning this communication should be directed to Jeffrey S. Parkin, Ph.D., whose telephone number is (571) 272-0908. The examiner can normally be reached Monday through Thursday from 10:30 AM to 9:00 PM. A message may be left on the examiner's voice mail service. If attempts to reach the examiner are unsuccessful, the examiner's supervisor, James C. Housel, can be reached at (571) 272-0902. Direct general status inquiries to the Technology Center 1600 receptionist at (571) 272-1600. Informal communications may be submitted to the Examiner's RightFAX account at (571) 273-0908.

Applicants are reminded that the United States Patent and Trademark Office (Office) requires most patent related correspondence to be: **a)** faxed to the Central FAX number (571-273-8300) (updated as of July 15, 2005), **b)** hand carried or delivered to the Customer Service Window (now located at the Randolph Building, 401 Dulany Street, Alexandria, VA 22314), **c)** mailed to the mailing address set forth in 37 C.F.R. § 1.1 (e.g., P.O. Box 1450, Alexandria, VA 22313-1450), or **d)** transmitted to the Office using the Office's Electronic Filing System. This notice replaces all prior Office notices specifying a specific fax number or hand carry address for certain patent related correspondence. For further information refer to the Updated Notice of Centralized

Delivery and Facsimile Transmission Policy for Patent Related Correspondence, and Exceptions Thereto, 1292 Off. Gaz. Pat. Office 186 (March 29, 2005).

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Respectfully,

Jeffrey S. Parkin, Ph.D.
Primary Examiner
Art Unit 1648

24 July, 2005